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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/152,698	Applicant(s) Madiyalakan et al
	Examiner Karen Canella	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *30, 71, 73-76, 85-89, and 91-97* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *30, 71, 73-76, 85-89, and 91-97* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☒ Interview Summary (PTO-413) Paper No(s). *16*
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. After review and reconsideration, the finality of the Office action of Paper No. 14 is withdrawn.

2. Claims 61-63, 66, 67, 69, 72, 77-84 and 90 have been canceled. Claims 30 and 71 have been amended. Claims 30, 71, 73-76, 85-89 and 91-97 are pending and under consideration.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

4. It is noted that applicant is claiming benefit to 09/094,598, filed June 15, 1998, now abandoned, 08/877,515, now U.S. 6, 086, 873, filed June 17, 1997 and 08/913,290, now U.S. 6, 241, 985, filed May 15, 1996. After review and reconsideration, it has be determined that the instant claims 30, 71, 73, 74, 76, 85-87, 89 and 91, 92, 94-97 will be given the priority date of the 09/094,598 application which contemplates the broadly claimed genus of "soluble antigen" and the species of "drugs of abuse", multiple sclerosis, allergy, "human immunodeficiency virus", bacterial infection and asthma, which are specific embodiments of the genus of "soluble antigens" or antigens. Further, the 09/094,598 application contemplates the AR20.5 monoclonal antibody. Neither of the 08/877,515 or the 08/913,290 application provide support for method claims based on this broad genus of soluble antigens, because both applications discuss only antibodies which bind to tumor associated antigens and the therapy of cancer or tumors. Claim 88 drawn to compositions comprising the monoclonal antibody B43.13 and claims 75 and 93, limited to methods of stimulating the production of antibodies which bind to epitopes on cancer cells, and compositions for treating cancers will be given the earlier priority date of May 15, 1996.

5. Claims 74 and 92 are objected to because of the following informalities: the markush group is identified as comprising species of "human diseases or conditions" and accordingly lists

cancer, tumor, multiple sclerosis, allergy bacterial infection, autoimmune disease and asthma. However, the Markush group also lists "drugs of abuse", "human immunodeficiency virus" and "human virus". These terms are the causes of human diseases or conditions, rather than the disease or conditions itself. Amendment of the Markush group to recite ---drug abuse, human immunodeficiency syndrome and human viral infection--- would overcome this objection.. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 30, 71, 73-76, 88, 89 and 94 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30 recites "Ab1". The art recognizes Ab1 as an antibody endogenous formed in response to the introduction of a foreign antigen. This nomenclature is used in reference to the idiotypic network. It is unclear how a foreign antibody can be an Ab1 antibody when administered directly to a host, because said host will recognize the foreign antibody as an antigen and generate an endogenous Ab1 antibody against said foreign antibody. Thus, it is unclear what constitutes an AB1 antibody in reference to the administration of said antibody to a foreign host. The metes and bounds of the claims cannot be determined as any foreign antibody from a foreign idiotypic network (Ab1, Ab2, Ab3, etc) will act as an antigen in said host, therefore the specification of an "Ab1" antibody for administration does not limit the scope of foreign antibodies which are encompassed by the claims. The designation of mAb1 versus mAb2 or mAb3 can only define the antibody in term of the relative position of a monoclonal antibody within the idiotypic network generated within a host. Thus, the designation of "mAb1" does not set the metes and bounds of the monoclonal antibody.

Claim 71 recites "wherein the foreign antibody is selected from the group consisting of ....a peptide; and a protein". The specification defines binding agent to include tumor binding peptides, receptor proteins, glycoproteins, lymphokines, cytokines, enzymes, immune modulators, and hormones (page 23, lines 18-22). It is unclear how any of these peptides and proteins can be a foreign antibody as required by claim 71.

Claims 88 and 89 are vague and indefinite in the recitation of B43.13 and AR20.5 as the only means of identifying the monoclonal antibodies on which the claimed methods depend. The use of laboratory designations only to identify a particular antibody/cell line renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct hybridomas and antibodies. Amendment of the claims to include the depository accession number of the mAb or hybridoma is required, because deposit accession numbers are unique identifiers which unambiguously define a given hybridoma and/or monoclonal antibody.

It is unclear how the specific limitation of "soluble" as recited in claim 94 applies to the composition comprising the antigen and the binding agent of claim 85, as the claim requires the formation of a complex of the binding agent and the antigen. It is unclear if claim 95 intends to define the solubility of the antigen before it complexes to the binding agent or if claim 95 intends that the complex of the antigen and the binding agent is soluble. For purpose of examination, both alternatives will be considered.

8. Claims 30, 71, 73-76, 85-87 and 91-97 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

(A) As drawn to new matter

Claims 30, 71 and 73-76 are rejected for the incorporation of new matter. Claim 30 has been amended to recite a "foreign mAb1 antibody" to replace "a foreign binding agent". The substitution of "monoclonal antibody" for "binding agent" more accurately reflects the metes and bounds of the methods of stimulating the production of an immune response comprising the administration of murine antibodies which react with human soluble antigens. However, the adjective "mAb1" does not find support within the specification as filed which teaches that any antibody generated in a non-human host would be useful in the claimed methods. The specification provides examples of the generation of an anti-idiotypic immune response wherein the first antibody is Ab1, however, this does not provide support for the amendment of claim 30 to restrict the invention to the administration of mAb1 versus any foreign monoclonal antibody.

(B) As drawn to written description

Claims 30, 71, 73, 74, 76, 85-87 and 91-97 are rejected for lacking adequate written description.

Claims 30 and 71 are method claims reliant upon the identity of a genus of soluble antigens. Dependent claim 74 specifies human diseases or conditions of cancer, tumor, drugs of abuse, multiple sclerosis, allergy, human immunodeficiency virus, bacterial infection, autoimmune disease, human viruses and asthma. Claim 85 is drawn to a composition comprising a binding agent and an antigen, wherein the binding agent and the antigen form a complex and wherein the administration of the complex to the host alters the host immune response against the antigen. Dependent claim 92 specifies the diseases or condition of cancer, tumor, drugs of abuse, multiple sclerosis, allergy, human immunodeficiency virus, bacterial infection, autoimmune disease, human viruses and asthma. The specification provides written description for two antibodies B43.13 and AR20.5 which bind to the human tumor antigens of CA-1245 and MUC1, respectively. The specification does not provide written description for any other antibodies which would bind antigens associated with the broadly claimed diseases or conditions of drugs of abuse, multiple sclerosis, allergy, human immunodeficiency virus,

bacterial infection, autoimmune disease, human viruses and asthma. Although it is routine to raise antibodies against antigens, the specification does not provide adequate written description for the multiple genuses of antigens. The disclosure of the mAb B43.13 and AR20.5 anticipate the genus of antigens comprising CA-125 and the genus of antigens comprising MUC1, however, the specification lacks adequate written description for the antigens associated with the genuses of drugs of abuse, multiple sclerosis, allergy, human immunodeficiency virus, bacterial infection, autoimmune disease, human viruses and asthma in addition to the broadly claimed genuses of cancer and tumors which comprise a multiplicity of antigens beyond those of MUC1 and CA-125, including antigens which have yet to be discovered. One of skill in the art would conclude that applicant has failed to disclose a representative number of species to anticipate each of the claimed genuses, therefore applicant was not in possession of the claimed genuses.

9. Claims 85, 86, 91, 92, 94, 95 and 97 are rejected under 35 U.S.C. 102(b) as being anticipated by Morgan et al (4,879,225, cited in a previous Office action).

Claim 85 is drawn to a composition for altering immunogenicity comprising an antigen and a binding agent that specifically binds to the antigen, wherein the binding agent and the antigen form a complex, and wherein administration of the composition to the host alters the host immune response against the antigen. Claim 86 is drawn in part to the composition of claim 85 wherein the binding agent is a protein. Claim 91 embodies the composition of claim 85 wherein the antigen is associated with a human disease or condition. Claim 92 is drawn in part to composition of claim 91 wherein the human disease or condition is selected from the group consisting of cancer and tumor. Claims 94 and 95 embody the composition of claim 85 wherein the antigen is a multi-epitopic antigen, a soluble antigen, respectively. Claim 97 embodies the composition of claim 85 wherein forming a complex between the binding agent and the antigen comprises exposing a previously inaccessible epitope on the antigen.

Morgan et al disclose a method for the enhanced production of antibodies using immune complexes consisting of pre-formed complexes comprising a binding agent and an antigen injected into a host, wherein the host generates antibodies to the epitopes on the antigen which are not masked in the antibody-antigen complex (column 6, lines 55-59). Morgan et al disclose that the method is an improvement in the prior art for generating antibodies to soluble immunogens which are weakly immunogenic (column 3, line 58 to column 4, line 3 and column 6, lines 47-51). Morgan et al disclose that the method provides a way to generate monoclonal antibodies against a multi-epitopic antigen (column 3, lines 28-31). Morgan et al do not specifically disclose that this method would generate antibodies to cryptic epitopes, however, antibodies to said cryptic epitopes would not be excluded by this method as all epitopes not masked in the first antibody-antigen complex would be available as antigenic epitopes in the host. Further, Morgan et al disclose that this method is useful for generating monoclonal antibodies directed to tumor-associated epitopes of non-tumor associated antigens. Thus Morgan et al disclose a method for the generation of antibodies to soluble antigens, multi-epitopic antigens and a method for the discovery of novel epitopes on tumor antigens which is commensurate with the unmasking of a cryptic epitope on a tumor associated or other antigen.

10. Claims 30, 71, 73-76 are rejected under 35 U.S.C. 102(b) as being anticipated by Baum et al (Cancer, 1994, vol. 73 (3 suppl), pp. 1121-1125) as evidenced by Madiyalakan et al (Hybridoma, 1995, Vol. 14, pp. 199-203, reference A2 of the I.D.S. filed March 20, 2000) or Madiyalakan et al (Hybridoma, 1995, Vol. 14, pp. 199-203).

Claim 30 is drawn to a method of stimulating the production of antibodies that bind to an epitope of a soluble antigen comprising administering to a host a foreign Ab1 that binds to the soluble antigen,; forming a complex between the foreign Ab1 wherein the formation of the complex exposes an epitope that is unexposed which the foreign Ab1 is not complexed with the antigen, and allowing the host to generate antibodies that bind to the exposed epitope. Claim 71

embodies the method of claim 30, wherein the foreign Ab1 is selected in part from the group consisting of an antibody, a monoclonal antibody and an antibody fragment. Claim 73 embodies the method of claim 30 wherein the soluble antigen is associated with a human disease or condition. Claim 74 embodies the method of claim 73 wherein the human disease or condition is selected from the group consisting of cancer and tumors. Claim 75 embodies the method of claim 74 wherein the cancer is selected from ovarian cancer. Claim 76 embodies the method of claim 30 wherein the host is human.

Baum et al disclose a method for treating ovarian cancer comprising the administration of F(ab')2 fragments of OC-125 or intact anti-MoAb B43.13 (page 1122, first column, under the heading "Monoclonal Antibodies"). Baum et al do not specifically disclose that said monoclonal antibody or antibody fragment would bind to a soluble antigen, however, the solubility of the CA-125 antigen would be inherent in the method of Baum et al as evidenced by Madiyalakan et al (who disclose that the idiotype induction was directly correlated with the level of CA-125 in the serum of the patients (page 203, first column, lines 4-10). Thus, the ovarian cancer patients treated by the method of Baum et al would include patients having soluble CA-125 antigen.

Madiyalakan et al disclose a method of stimulating the production of anti-idiotypic antibodies that bind to an epitope on a soluble antigen comprising the administration of the murine monoclonal antibody B43.13 to human patients having ovarian carcinoma. Madiyalakan et al disclose that the idiotype induction was directly correlated with the level of CA-125 in the serum of the patients (page 203, first column, lines 4-10).

Neither Madiyalakan et al nor Baum et al specifically disclose that the host would generate antibodies to an epitope which was exposed after binding of the antibody, however, Baum et al and Madiyalakan et al disclose a method comprising the administration of the same antibody (B43.13) and antigen (CA-125) as taught by the instant specification, thus both of the prior art methods would inherently result in the generation of antibodies that bind to exposed

epitopes on the CA-125 antigen, as the instant method comprises the same steps as the prior art methods.

11. Claims 30, 71, 73-76 are rejected under 35 U.S.C. 102(b) as being anticipated by Wagner et al (Biotechnology Therapeutics, 1992, Vol. 3, pp. 81-89) as evidenced by Madiyalakan et al (Hybridoma, 1995, Vol. 14, pp. 199-203). The specific embodiments of the claims are set forth above.

Wagner et al disclose a method of stimulating the production of antibodies that bind to an epitope on CA-125 comprising the administration of F(ab)2 fragment of the monoclonal antibody OC 125 (page 83, under "Patients and Methods"). Wagner et al disclose that the activation of the anti-idiotypic network was performed in patients with preoperatively high plasma values of CA-125 (page 84, lines 6-9). Madiyalakan et al disclose that the idiotype induction against the CA-125 antigen in ovarian cancer patients was directly correlated with the level of CA-125 in the serum of the patients (page 203, first column, lines 4-10). Wagner et al do not specifically teach that the host would generate antibodies to an epitope which was exposed after binding of the antibody, however, Wagner et al disclose a murine antibody which binds to the same antigen (CA-125) as taught by the instant specification, thus the method disclosed by Wagner et al would inherently result in the generation of antibodies that bind to exposed epitopes on the CA-125 antigen, as the method comprises the same steps as claimed.

12. Claims 30, 71, 73-75 are rejected under 35 U.S.C. 102(e) as being anticipated by Diamandis et al (U.S. 6,068,830) as evidenced by Schwartz, ("Cancer Markers", In: Cancer: Principles and Practice of Clinical Oncology, 4th Edition, 1994, DeVita et al, Ed.s., page 531-542). The specific embodiments of the claims are set forth above., with the addition that claim 75 also embodies breast cancer.

Diamandis et al disclose a method of comprising the administration of antibodies which specifically bind to PSA for the treatment of cancers such as breast cancer, which expresses ans secrete the antigen of PSA (column 5, lines 52-65 and column 9, lines 41-48). Diamandis et al disclose the production of anti-idiotypic antibodies as a result of the administration of anti-PSA antibodies (column 9, lines 51-59). Schwartz et al disclose that PSA is a soluble tumor antigen in prostate cancer (Table 21-5). Additionally, Diamandis et al disclose that PSA is detected in culture supernatant of breast cancer cells, thus it is reasonable to conclude that patients having breast cancer cells which express PSA in vivo also have PSA as a soluble antigen in vivo. Diamandis et al do not specifically teach that the host would generate antibodies to an epitope which was exposed after binding of the antibody, however the claimed method appears to be inherently the same as the prior art method, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art method does not result in an exposure of previously unexposed after binding of the antibody. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

13. Claims 30, 71 and 73-76 are rejected under 35 U.S.C. 102(b) as being anticipated by Goldenberg et al ("Cancer Diagnosis and Therapy with Radiolabeled Antibodies", In: Immunoconjugates, Antibody Conjugates in Radioimaging and Therapy of Cancer, Vogel. Ed., 1987, pages 259-280) as evidenced by Schwartz et al ("Cancer Markers" In: Cancer: Principles and Practice of Oncology, DeVita et al, Ed.s, 4th edition, 1993, pp. 531-542). The specific embodiments of the claims are set forth above., with the addition that claim 75 also embodies gastro-intestinal cancer.

Goldenberg et al disclose a method comprising the administration of an anti-PAP, anti-CEA or an anti-AFP antibody to patients having ovarian, breast and gastrointestinal cancers (page 263, lines 10-21 under the heading "Cancer Imaging Markers"). Goldenberg et al disclose that the human cancer patients have high levels of circulating CEA (page 261, , lines 31-35). Goldenberg et al also disclose that AFP (alpha fetoprotein) is also a soluble tumor antigen (page 264, lines 12-16). Schwartz et al disclose that PAP is a soluble tumor marker in prostate cancer (table 21-5).

Goldenberg et al do not specifically teach that the host would generate antibodies to an epitope which was exposed after binding of the antibody, however the claimed method appears to be inherently the same as the prior art method, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art method does not result in an exposure of previously unexposed after binding of the antibody. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

14. Claims 30, 71, 73, 74 and 76 are rejected under 35 U.S.C. 102(b) as being anticipated by Courtenay-Luck (U.S. 5,591,593). Claim 75 is rejected under 35 U.S.C. 102(e) as being anticipated by Courtenay-Luck (U.S. 5,591,593). The specific embodiments of the claims are set forth above

It is noted that claim 75 has a priority date of May 15, 1996 in contrast to claims 30, 71, 73, 74 and 76 which have the priory date of June 15, 1998.

Courtenay-Luck et al disclose antibodies having the minimum recognition unit of "EPPT" which specifically bind to mucins (column 3, lines 6-9, lines 21-29). Courtenay-Luck et al disclose a method for treating cancer comprising the administration of said antibodies "alone"

(column 4, lines 7-13). Courtenay-Luck et al disclose that said mucins are shed from tumor cells and thus are soluble antigens (column 3, lines 57-58). Courtenay-Luck et al do not specifically teach that the host would generate antibodies to an epitope which was exposed after binding of the antibody, however the claimed method appears to be inherently the same as the prior art method, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art method does not result in an exposure of previously unexposed after binding of the antibody. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

15. Claims 30, 71, 73, 74 and 76 are rejected under 35 U.S.C. 102(b) as being anticipated by Byers et al (U.S. 5,512,283). The specific embodiments of the claims are set forth above with addition that claim 74 further encompasses asthma.

Byers et al disclose a method of stimulating the production of anti-idiotypic antibodies comprising the administration of the monoclonal antibody of H11 or a monoclonal antibody which recognizes the same epitope as H11 (column 11, lines 42-55 and claims 1 and 2). Byers et al do not specifically teach that the host would generate antibodies to an epitope which was exposed after binding of the antibody, however the claimed method appears to be inherently the same as the prior art method, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art method does not result in an exposure of previously unexposed after binding of the antibody. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish

patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

16. Claims 85, 86, 91 and 92, 93 and 96 are rejected under 35 U.S.C. 102(e) as being anticipated by Storkus et al (U.S. 6,077,519).

Claim 85 is drawn to a composition for altering immunogenicity comprising an antigen and a binding agent, wherein the binding agent and the antigen form a complex, and wherein administration of the composition to a host alters the host immune response against the antigen. Claim 86 embodies the composition of claim 85 wherein the binding agent is in part selected from a peptide. Claim 91 embodies the composition of claim 85 wherein the antigen is associated with a human disease or condition. Claim 92 embodies the composition of claim 91 wherein the human disease or condition is selected in part from cancer or tumor. Claim 93 embodies the composition of claim 92 wherein the human disease or condition is selected in part from gastro-intestinal cancer. Claim 96 embodies the composition of claim 85 wherein the host is human.

Storkus et al disclose a composition comprising a dendritic cell and a peptide, wherein the dendritic cell and the peptide form a complex in the context of the MHC on the dendritic cells. Storkus et al disclose the administration of said peptide-pulsed dendritic cells for the treatment of advanced malignancies including colo-rectal cancer (column 45, line 9 to column 46, line 32). Thus the administration of the peptide-pulsed dendritic cells disclosed by Storkus et al alters the immune response of the host against the peptide, fulfilling all of the claimed embodiments.

17. Claims 85-87, 91, 92, 94, 95 and 96 are rejected under 35 U.S.C. 102(b) as being anticipated by St Remy et al (U.S. 4,740,371). The specific embodiments of claims 85, 86, 91, 92 and 96 are recited above, with the exception that claim 92 further embodies the composition

of claim 91 wherein the human disease or condition is selected in part from asthma. Claim 94 embodies the composition of claim 85 wherein the antigen is a multi-epitopic antigen. Claim 95 embodies the composition of claim 85 wherein the antigen is a soluble antigen.

St.Remy et al disclose a composition comprising an antigen and an antibody directed against said antigen for the down regulation of the IgE immune response against said antigen (column 3, lines 25-39). St.Remy et al disclose that the antibody can be polyclonal or monoclonal (column 4, line 66), thus fulfilling the specific embodiments of claims 86 and 87). St.Remy et al disclose that patients can be treated for allergic asthma caused by house dust mites (column 6, lines 54-56) fulfilling the specific embodiment of asthma in claim 92. St.Remy disclose that commercially available allergens were purified by gel filtration chromatography (column 7, lines 47-50), therefore it is reasonable to conclude that the antigens were soluble, fulfilling the specific embodiment of claim 95. St.Remy states that the use of polyclonal antibodies are preferable as they avoid the risk of allergic reactions against unmasked antigenic determinants (column 4, line 66 to column 5, line 3), thus, it is reasonable to conclude that the antigens are multi-epitopic. St.Remy do not specifically teach that the host would generate antibodies to an epitope which was exposed after binding of the antibody, however the claimed composition appears to be the same as the prior art composition, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art composition does not result in an exposure of previously inaccessible previously unexposed after binding of the antibody. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

18. Claims 85, 86, 91, 92, 96 are rejected under 35 U.S.C. 102(b) as being anticipated by Berzofsky et al (WO 94/21287). The specific embodiments of the claims are recited above with the exception that claim 92 further comprises human immunodeficiency virus and human viruses. .

Berzofsky et al disclose a composition comprising dendritic cells pulsed with peptides comprising an immunodominant determinate for CTL in the gp1260 envelope protein of HIV-1 (page 32-48), wherein administration of said composition to a host alters the host immune response against the antigen in that CD+8 CTL are induced (example II, page 32-48). The peptide would be bound by a binding agent which was a MHC peptide on the surface of the dendritic cell (page 46, lines 9-12), thus fulfilling the specific embodiment of claim 86 drawn to a peptide. Berzofsky et al disclose the administration of said peptide-pulsed dendritic cells to specific patients for immunotherapy (page 47, lines 33-36), thus fulfilling the specific embodiments of claim 96, drawn to a human host.

19. Claims 85, 86, 91-93 and 96 are rejected under 35 U.S.C. 102(e) as being anticipated by Cheever et al (U.S. 5,869,445, priority to March 31, 1995). The specific embodiments of claims 85, 86, 91 and 92, 93 and 96 are set forth above. Claim 93 also comprises breast cancer.

Cheever et al disclose a composition comprising dendritic cells pulsed with a human her-2/neu polypeptide (column 20, lines 1-24), wherein the administration of said dendritic cells elicits a cellular immune response in a patient, including human patients (column 16, line 62 to column 17, line 10). Cheever et al teach that said pulsed dendritic cells were able to activate in vitro CD+4 T lymphocytes from normal human donors (column 20, lines 25-51) as well as in CD+4 lymphocytes from breast cancer patients (column 23, line 25 to column 24, line 17).

20. Claims 30, 71, 73-76, 85-88 and 91-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Madiyalakan et al (Hybridoma, 1995, Vol. 14, pp. 199-203) in view of Klaus

(Nature, 1978, vol. 272, pp. 265-266, cited in a previous Office action) and the abstract of Bachmann et al (European Journal of Immunology, 1994, Vol. 24, pp. 2567-2570). The specific embodiments of the claims are recited above.

Madiyalakan et al teach the specific embodiments of claims 30, 71, 73-76 for the reasons set forth in the rejection under 102(b), above. Madiyalakn et al teach that the induction of the anti-idiotypic network by the anti-CA125 antibody is correlated to the presence of circulating CA125 antigen. Madiyalakan et al do not teach a composition comprising an antigen and a binding agent, wherein the binding agent and the antigen form a complex.

Klaus teaches that it is necessary for the audiotape of antibodies to be markedly immunogenic in order for the induction of anti-idiotypic antibody production (page 265, lines 7-9 under title). Klaus teaches antibodies only acquire marked immunogenicity when complexed with the eliciting antigen (page 266, second column, lines 1-4). Klaus teaches that immunogenicity of antigen-antibody complexes is dues to rapid localization of said complexes to the lymphoid follicles (page 266, first column, lines 29-36).

The abstract of Bachmann et al teaches that the amount of persisting antigen-antibody complexes within the follicular dendritic cells is correlated to the persistence of protective IgG response.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to administer the B43.13 antibody complexed with CA125 to ovarian cancer patients in order to stimulate the production of the anti-idiotypic network. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of

a. Madiyalakan et al on the correlation between the induction of the anti-idiotypic network and survival after administration of the B43.13 antibody, and the further correlation between the induction of the anti-idiotypic network and the presence of circulating CA125;

b. Klaus on the induction of the anti-idiotypic network by means of an antibody-antigen complex versus the antibody alone, and the teachings of Klaus that antibody-antigen complexes are rapidly localized in the lymphoid follicles;

c. The abstract of Bachman et al on the correlation between the persistence of antibody-antigen complexes within follicular dendritic cells and the persistence of a protective IgG response.

One of skill in the art would be motivated to administer the B43.13 antibody as an antibody-antigen complex rather than as an antibody alone, in order to cause rapid localization and persistence in the follicular dendritic cells, thus inducing anti-idiotype antibody formation and persistence of the resulting protective anti-idiotypic immune response.

21. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

22. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentable distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. *In re Berg*, 140 F. 3d 1428, 46 USPQ2d 1226 (Fed Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

23. Claims 30, 73-76, 85-88 and 91-97 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 5, 10, 14-37 of copending Application No. 09/641,833 in view of Madiyalakan et al (Hybridoma, 1995, Vol. 14, pp. 199-203) in view of Klaus (Nature, 1978, Vol. 272, pp. 265-266) and the abstract of Bachmann et al (European Journal of Immunology, 1994, Vol. 24, pp. 2567-2570) and the abstract of Yin et al (International Journal of Cancer, 1996, Vol. 65, pp. 406-412) and the abstract of McGuckin et al (Clinica Chimica Acta, 1993, Vol. 214, pp. 139-151). Claim 1 of the '833 application is drawn to a therapeutic composition consisting essentially of a binding agent that bid to an epitope of MUC-1 and is effective in therapeutically treating a mammal having a tumor that expresses MUC-1. Claim 2 is drawn to a therapeutic composition other than HMFG1 that specifically binds to an epitope of MUC-1, and is effective in therapeutically treating a mammal having a tumor that expresses MUC-1. Claim 3 is drawn to a therapeutic composition that binds to both a soluble and tumor associated MUC-1 and is effective in therapeutically treating a mammal having a tumor that expresses MUC-1. Claim 5 is drawn to the therapeutic compositions of claims 1, 2 or 3 wherein the binding agent induces an anti-idiotypic response and a cellular immune response in the mammal. Claim 10 is drawn to a therapeutic composition comprising an activated binding agent that specifically binds to an epitope of tumor associated MUC-1 and is effective in therapeutically treating a mammal having a tumor that expresses MUC-1. The therapeutic composition of claims 1 or 2 wherein the epitope comprises an immunological determinant that includes carbohydrate.

Claim 15 is drawn in part to a method of treatment comprising the administration of the composition of claims 1-3, 5 and 10. Claims 16-35 and 37-39 are drawn to methods of treatment comprising administering a binding agent that binds MUC-1.

Madiyalakn et al teach that the induction of the anti-idiotypic network by the anti-CA125 antibody is correlated to the presence of circulating CA125 antigen. Madiyalakan et al do not teach a composition comprising an antigen and a binding agent, wherein the binding agent and the antigen form a complex.

Klaus teaches that it is necessary for the audiotape of antibodies to be markedly immunogenic in order for the induction of anti-idiotypic antibody production (page 265, lines 7-9 under title). Klaus teaches antibodies only acquire marked immunogenicity when complexed with the eliciting antigen (page 266, second column, lines 1-4). Klaus teaches that immunogenicity of antigen-antibody complexes is dues to rapid localization of said complexes to the lymphoid follicles (page 266, first column, lines 29-36).

The abstract of Bachmann et al teaches that the amount of persisting antigen-antibody complexes within the follicular dendritic cells is correlated to the persistence of protective IgG response.

The abstract of Yin et al identifies MUC-1 as one of the two major ovarian cancer antigens along with CA125.

The abstract of McGuckin et al teaches that tumor -associated MUC-1 is a soluble antigen as it is detected in the serum.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to make a composition comprising a binding agent and MUC-1 wherein the binding agent was an anti-MUC-1 antibody and wherein the anti-MUC-1 antibody was complexed to MUC-1. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of

a. Madiyalakan et al on the correlation between the induction of the anti-idiotypic network and survival after administration of the B43.13 antibody, and the further correlation between the induction of the anti-idiotypic network and the presence of circulating CA125;

b. Klaus on the induction of the anti-idiotypic network by means of an antibody-antigen complex versus the antibody alone, and the teachings of Klaus that antibody-antigen complexes are rapidly localized in the lymphoid follicles;

c. The abstract of Bachman et al on the correlation between the persistence of antibody-antigen complexes within follicular dendritic cells and the persistence of a protective IgG response

d. The abstract of Yin et al which identifies MUC-1 as a major ovarian cancer antigen along with CA125,

e. The abstract of McGuckin et al which identifies MUC-1 as a soluble antigen.

One of skill in the art would be motivated to combine the therapeutic compositions of claims 1-3, 5, 10, 14-37 of copending Application No. 09/641,833 with the teachings of Madiyalakan et al and Klaus and the abstract of Bachman et al in order to make a therapeutic composition which would anticipate the instant claims 85-88 and 91-97 and administer said compositions in a method of treatment which would anticipate instant claims 30, 73-76.

This is a provisional obviousness-type double patenting rejection.

24. The rejection of claims 30, 71, 73-76, 85-89, 91-97 under the judicially created doctrine of double patenting over claims 1-14 of U. S. Patent No. 6,241,985 is maintained for reasons of record. Applicant states that a terminal disclaimer which overcomes the instant rejection was provided in the response filed October 29, 2002. Upon review of said response, it is noted that a terminal disclaimer was not included with the papers filed on that date or subsequent to said date.

25. The declaration filed January 7, 2002, naming the instant inventors of Madiyalakan, Noujaim, Baum and Schultes as inventors remains defective as it is unexecuted. Please provide a signed declaration.

26. All other rejections and objections as set forth in Paper No. 14 are withdrawn.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella

Karen A. Canella, Ph.D.

Patent Examiner, Group 1642

July 21, 2003